



Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Center – WO66-G609  
Silver Spring, MD 20993-0002

November 6, 2014

AEROCRINE  
SUSANNE PARKS, DIRECTOR, RA & QA  
P. O. BOX 1024  
RÅSUNDAVÄGEN 18, 8TH FLOOR  
SE-171 21 SOLNA, SWEDEN

Re: K133898  
Trade/Device Name: NIOX VERO®  
Regulation Number: 21 CFR 862.3080  
Regulation Name: Breath nitric oxide test system  
Regulatory Class: II  
Product Code: MXA  
Dated: September 23, 2014  
Received: September 24, 2014

Dear Ms. Susanne Parks:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

 Courtney H. Lias -S

Courtney H. Lias, Ph.D.  
Director  
Division of Chemistry and Toxicology Devices  
Office of In Vitro Diagnostics  
and Radiological Health  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)

K133898

Device Name

NIOX VERO

Indications for Use (Describe)

NIOX VERO® measures Nitric Oxide (NO) in human breath. Nitric Oxide is frequently increased in some inflammatory processes such as asthma. The fractional NO concentration in expired breath (FeNO), can be measured by NIOX VERO according to guidelines for NO measurement established by the American Thoracic Society.

Measurement of FeNO by NIOX VERO is a quantitative, non-invasive, simple and safe method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. NIOX VERO is suitable for children, approximately 7 - 17 years, and adults 18 years and older.

FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NIOX VERO is intended for prescription use and should only be used as directed in the NIOX VERO User Manual by trained healthcare professionals. NIOX VERO cannot be used with infants or by children approximately under the age of 7, as measurement requires patient cooperation. NIOX VERO should not be used in critical care, emergency care or in anesthesiology.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

**\*DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.\***

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
Paperwork Reduction Act (PRA) Staff  
[PRASStaff@fda.hhs.gov](mailto:PRASStaff@fda.hhs.gov)

*"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."*

## **TRADITIONAL 510(k) SUMMARY**

The assigned 510(k) number is: k133898

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SDMA 1990 and 21 CFR 807.92.

**Preparation Date:** November 4, 2014

**510(k) Applicant:** Aerocrine AB  
Råsundavägen 18, 8th Floor  
SE-171-21 Solna, Sweden  
Phone: +46-8-629-0780  
Fax: +46-8-629-0781

**Contact Person:** Susanne Parks  
Director Regulatory Affairs & Quality Assurance

**Trade Name:** NIOX VERO®  
**Common Name:** Airway Inflammation Monitor  
**Classification Name:** System, Test, Breath Nitric Oxide  
**Regulatory Class:** Class II  
**Product Code:** MXA  
**CFR Section:** 21 CFR 862.3080

**Predicate Device:** NIOX MINO® Airway Inflammation Monitor  
**510(k) Clearance Number:** K101034  
Class II under 21 CFR 862.3080, Product Code MXA

**510(k) Applicant:** Aerocrine AB  
Råsundavägen 18, 8th Floor  
SE-171-21 Solna, Sweden  
Phone: +46-8-629-0780  
Fax: +46-8-629-0781

## Device Description

NIOX VERO is a portable system for the non-invasive, quantitative measurement of the fraction of exhaled nitric oxide (NO) in expired human breath (FeNO). NO levels increase during allergic airway inflammation. Measurement of changes in FeNO concentration is used in evaluating a patient's response to anti-inflammatory therapy, as an adjunct to established clinical and laboratory assessments.

The NIOX VERO system is comprised of the NIOX VERO unit with AC adapter, a rechargeable battery, an electrochemical NO sensor, disposable patient filters, and an exchangeable handle containing an internal NO scrubber filter. The NIOX Panel is an optional PC application for operation of the NIOX VERO from a PC and access to electronic medical record systems.

The patient empties their lungs, inhales deeply through the patient filter to total lung capacity and then slowly exhale for 10 seconds. In approximately one minute, the NO concentration is displayed in parts per billion (ppb).

The NIOX VERO unit includes a sampling and gas conditioning system and a man-machine interface (MMI). The instrument controls the inhaled sample appropriately via the electronics and software program. Filtering of inhaled air eliminates contamination from ambient NO levels. A built-in flow control keeps exhalation standardized at 50 ml/s so that it is standardized for all patients. The sample enters an electromechanical sensor and interacts with an electrolyte. A chemical reaction takes place where electrons are generated proportional to the number of NO molecules.

Results are processed using dedicated software. In order to verify the device's performance and reliability of measurements, there are built-in system control procedures and a Quality Control procedure to be performed on a daily basis.

## Intended Use/Indications for Use

NIOX VERO® measures Nitric Oxide (NO) in human breath. Nitric Oxide is frequently increased in some inflammatory processes such as asthma. The fractional NO concentration in expired breath (FeNO), can be measured by NIOX VERO according to guidelines for NO measurement established by the American Thoracic Society.

Measurement of FeNO by NIOX VERO is a quantitative, non-invasive, simple and safe method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. NIOX VERO is suitable for children, approximately 7 - 17 years, and adults 18 years and older.

FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NIOX VERO is intended for prescription use and should only be used as directed in the NIOX VERO User Manual by trained healthcare professionals. NIOX VERO cannot be used with infants or by children approximately under the age of 7, as measurement requires patient cooperation. NIOX VERO should not be used in critical care, emergency care or in anesthesiology.

## **Technological Characteristics Compared to Predicate**

### **Similarities**

1. Analytical principle of electrochemical detection
2. NO sensor design and signal processing
3. The principle for sample collection and sample handling inside the instrument
4. Format of the measurement result in ppb
5. Process of patient sample collection method
6. The Quality Control procedure
7. The measurement performance specifications ( linearity, accuracy, precision, detection limit)
8. Elimination of ambient NO in patient inhalation and in sampling for baseline control
9. Use of a touchscreen to navigate the device and display a visual incentive for the user to follow.
10. Portable devices
11. Communication via USB with a PC
12. Internal measurement result storage.
13. The NIOX Panel is a software accessory used with both NIOX MINO and NIOX VERO.
14. Measurements are in accordance with ATS guidelines

### **Differences**

- 1) The device design was updated:
  - a. The touch screen is larger and in color in the NIOX VERO for ease of use.
  - b. The NIOX VERO can operate from battery power.
  - c. The patient filter attaches to a handle. This allows the patient to directly view the screen which enhances the device to aid the patient in generating a breath sample. The NO scrubber is now located in this handle which will be disposed of after the NO scrubber has expired.
  - d. Buffer chamber capacity is smaller.
  - e. Flow regulator is now electromechanical.
- 2) The instrument lifetime was extended to 5.5 years or 15,000 measurements.
- 3) The sensor stabilization process has been modified. Instead of maintaining the sensor at a constant temperature, there is a compensation algorithm for temperature and humidity correction to the measurement result.

## **PERFORMANCE TESTING**

Performance testing was conducted to demonstrate substantial equivalence between the NIOX VERO and the NIOX MINO (predicate device).

- 1) The NIOX VERO conforms to the same electrical safety and EMC performance standards as the predicate device, EN/IEC 60601-1 2<sup>nd</sup> edition (1988), 60601-1-2:2000).
- 2) The biocompatibility of the filter was assessed to the same performance standards as the predicate (ISO 10993-1:2003). Cytotoxicity, Sensitization, and Irritation/Intracutaneous reactivity tests were performed. All data indicated the patient filter was safe for use.
- 3) Software validation is performed according to FDA Guidance: General Principles of Software Validation, Final Guidance for Industry and Staff issued Jan 11, 2002. The NIOX VERO software is considered to be “Moderate Concern” software. IEC 62304 Medical Device Software-Software life Cycle Processes 2006-05 was also utilized.

Software verification and validation shows the device software and NIOX Panel meets design inputs requirements and user needs. The usability of the NIOX VERO has been validated.

- 4) Stability testing was performed on the device and the sensor.
- 5) A comparison study was performed between the NIOX MINO and the NIOX VERO which demonstrate substantial equivalence in a clinical setting.
- 6) Testing with potential interferents was performed.
- 7) Specific performance characteristics were developed for the NIOX VERO using Nitric Oxide gas samples at certified concentrations. The following testing was performed and results are compared to NIOX MINO.

	NIOX MINO (predicate)	NIOX VERO
Analytical limits at low levels, (limit of detection)	5 ppb	5 ppb
Precision	< 3 ppb of measured value for values < 30 ppb < 10% of measured value for values $\geq 30$ ppb	< 3 ppb of measured value for values < 30 ppb < 10% of measured value for values $\geq 30$ ppb
Accuracy	+/- 5 ppb or max 10%	+/- 5 ppb or max 10%
Measurement Range	5 - 300 ppb	5 - 300 ppb
Linearity, reportable range	Squared correlation coefficient $r^2 \geq 0.998$ , slope 0.95 – 1.05, intercept $\pm 3$ ppb	Squared correlation coefficient $r^2 \geq 0.998$ , slope 0.95 – 1.05, intercept $\pm 3$ ppb

## Conclusions:

The NIOX VERO has the same intended use as the predicate device, the NIOX MINO. The minor changes to the indications do not alter the intended diagnostic effect and do not impact the safety and effectiveness of the device. The device modifications do not affect the device's fundamental scientific technology. Performance testing demonstrates the NIOX VERO is substantially equivalent in technological characteristics and does not raise new questions of safety and effectiveness. Furthermore, the performance testing confirms that the NIOX VERO is at least as safe and effective as the NIOX MINO (predicate) device.